

CLAIMS

1. A composition comprising poly(D-L-lactide-co-glycolide) (PLGA) microspheres encapsulating an antigen, wherein

the ratio of lactide to glycolide is from about 100:1 to 1:100 weight percent;

the inherent viscosity of PLGA polymers used in the microspheres is about 0.1 to 1.2 dL/g;

the median diameter of the microspheres is from about 20 to 100  $\mu\text{m}$ ; and

the antigen is released from the microspheres in a triphasic pattern, wherein about 0.5 to 95% of the antigen is released in an initial burst, about 0 to 50% is released over a period of about 1 to 180 days, and the remaining antigen is released in a second burst after about 1 to 180 days.

2. The composition of claim 1 wherein the antigen is an HIV polypeptide.

3. The composition of claim 2 wherein the HIV polypeptide is gp120.

4. The composition of claim 1 wherein the median diameter of the microspheres is about 30  $\mu\text{m}$ .

5. The composition of claim 1 further comprising an adjuvant.

6. The composition of claim 5 wherein the adjuvant is encapsulated in the PLGA microspheres.

7. The composition of claim 5 wherein the adjuvant is coencapsulated with the antigen in the microspheres.

8. The composition of claim 5 wherein the adjuvant is QS21.

9. The composition of claim 1 further comprising a soluble antigen.

10. A composition for use as a vaccine comprising an antigen encapsulated in poly(D-L-lactide-co-glycolide) (PLGA) microspheres, and a soluble antigen.

11. A composition for use as a vaccine comprising about one to 100 antigens encapsulated in a mixture of about two to 50 poly(D-L-lactide-co-glycolide) (PLGA) microsphere populations, wherein

the ratio of lactide to glycolide is from about 100:1 to 1:100;

the inherent viscosity of PLGA polymers used in the microspheres is about 0.1 to 1.2 dL/g;

the median diameter of the microspheres is from about 20 to 100  $\mu\text{m}$ ; and

the antigen is released from the microspheres in a triphasic pattern, wherein about 0.5 to 95% of the antigen is released in an initial burst, about 0 to 50% is released over a period of about 1 to 180 days, and the remaining antigen is released in a second burst in one microsphere population after about 1 to 30 days, in a second microsphere population after about 30 to 90 days, and in additional microsphere populations after about 90 to 180 days.

12. The composition of claim 11, wherein each microsphere population encapsulates the same antigen.

13. A method for encapsulating antigen in microspheres, comprising

(a) dissolving poly(D-L-lactide-co-glycolide) (PLGA) polymer in an organic solvent to produce a solution;

(b) adding an antigen to the solution of (a) to produce a PLGA-antigen mixture comprising a first emulsion;

(c) adding the mixture of step (b) to an emulsification bath to produce microspheres comprising a second emulsion; and

(d) hardening the microspheres of step (c) to produce hardened microspheres comprising encapsulated antigen.

14. The method of claim 13 wherein the organic solvent is methylene chloride.

15. The method of claim 13 wherein the organic solvent is ethyl acetate.

16. The method of claim 13 wherein the organic solvent is a mixture of ethyl acetate and benzyl alcohol or acetone.

17. The method of claim 13 wherein the emulsification bath comprises a polyvinyl alcohol solution.

18. The method of claim 17 wherein the polyvinyl alcohol solution contains ethyl acetate.

19. The method of claim 13 wherein the antigen is a dry polypeptide.

20. The method of claim 13 wherein the antigen is aqueous.

21. The method of claim 13 further comprising drying the hardened microspheres.

22. The method of claim 21, wherein the drying is selected from the group consisting of lyophilizing, fluidized bed drying, and vacuum drying.

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